CASE REPORTS

An Early Fatal Case of Infantile Toxoplasmosis In California

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IT is the purpose of this presentation to report a case of toxoplasmosis in an infant from California, believed to be the earliest on record in the United States.

Neonatal cases of toxoplasmosis are being reported with greater frequency. Nearly 40 such cases, proven either by isolation of the organism, by autopsy, or by both methods, have been reported to date.[3, 12] Clinically, toxoplasmosis in the newborn may manifest itself by enlargement of the head due to internal hydrocephalus, by chorioretinitis, and by signs of central nervous system irritation, such as convulsions, spasticity, reflex changes and hypothermia. On ventricular puncture, xanthochromic fluid of high protein content (grams per 100 cc.) is usually obtained. Occasionally, toxoplasma can be visibly demonstrated in such fluid. More successful, usually, are attempts at isolation of the organism by animal inoculation.

The protein and cell contents of the subarachnoid and spinal fluid are likewise increased. However, the protein levels are in the range of hundreds of milligrams per 100 cc., rather than the thousands of milligrams per 100 cc. as in the ventricular fluid. On radiological examination of the skull, intracerebral calcifications may be found. The latter are not as common, however, as chorioretinitis, which has been found in almost every neonatal case of toxoplasmosis, properly investigated.

Such are the signs and symptoms of most of the fatal cases described.[10] However, in a few cases of neonatal toxoplasmosis there have been manifestations of disease referable mainly to the extraneural viscera, such as icterus due to hepatitis, anemia and disturbance of growth.[7, 8, 16] Here again, chorioretinitis is usually present, and on autopsy a diffuse involvement of all of the viscera has been found.[7, 8] Nevertheless, many of the infants showing the latter symptom complex survive,[1, 4] and it is this symptom complex that is sometimes elicited in children with signs of chronic toxoplasmosis dating back to early infancy. Those infants showing signs and symptoms referable to the central nervous system are thought to have passed through a state of generalized visceral infection earlier, usually *in utero*, after acquiring the infection by the transplacental route.[3]

The causative organism, *Toxoplasma gondii*, is generally regarded to be a protozoan. Its name is derived from the Greek *toxon*, meaning a bow or arc, and referring to the lunate shape of the organism in the fresh state. The specific name *gondii* is derived from the name of the host in which the organism was first observed. This was the gondi (*Ctenodactylus gondi*, Pallas, 1778), a small North African rodent, which was used as a laboratory animal at the Institute Pasteur of Tunis and from which Nicolle and Manceaux first described toxoplasma in 1908 and 1909.[6] The organism is known only to reproduce by binary fission. Proliferative forms and so-called "pseudocysts" can be distinguished. The individual organisms usually appear spherical on sections. The early literature on toxoplasmosis has been reviewed by Sabin[10] and Weinman.[14]

Recently, one of the authors (J.K.F.) observed two and collected reports of two further cases of fatal neonatal toxoplasmosis. When these cases were presented and were discussed by the other author (H.C.N.) he recalled a similar case, which he had observed 26 years ago. Slides, paraffin-blocks, as well as the eyes of the baby had been preserved, so it was not difficult to make the diagnosis even at this late date. Fortunately, too, the baby's parents could be contacted and they were kind enough to submit to skin and serological tests for toxoplasmosis.

CASE REPORT

The patient was born prematurely at Adler's Sanitarium, San Francisco, in 1923. The head was enlarged, the fontanelles were bulging and the cranial sutures were separated. Right microphthalmia was noted. Surgical incision through the scalp overlying the anterior fontanelle revealed a tense bulging dura. The convolutions were not remarkable. Puncture of both ventricles revealed thick and yellow fluid. The temperature was unstable and the baby died at the age of five days.

Autopsy Findings. The body was that of an underdeveloped male infant without rigor mortis. The fontanelles and sutures of the cranial bones were widely open. Over the anterior fontanelle, a silver foil dressing closing a recent 3 cm. long incision was present. The right eye was distinctly smaller than the left. No significant gross findings were noted regarding the thoracic and abdominal viscera. On removal of the brain from the calvarium a large amount of yellowish fluid was found, containing several large accumulations of thick, tenacious material and small fat droplets. The cerebral hemispheres collapsed during removal. The brain was small and had a yellowish appearance, with a number of white, somewhat granular areas. There was microgyria of the right occipital lobe.

Microscopic sections of the heart showed several foci of subsiding myocarditis (Figure 1). Mild interstitial pneumonitis, slight hepatitis, splenitis and interstitial nephritis were present. In both eyes, foci of retinal degeneration, cellular infiltration and toxoplasma were observed (Figures 2 and 3). No brain material had been saved. A more detailed histopathological report will be made at a later date.

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Skin Tests and Serological Findings on the Parents. Twenty-five years after giving birth to the patient the mother proved to have positive reaction for Toxoplasma gondii by both the toxoplasmin skin test[2] and the toxoplasma neutralizing antibody test. The latter was positive as performed in the rabbit skin,[9] and an in vitro titer of 1:64 was obtained.[11] Reaction to skin test of the father, while negative at 40 hours, turned positive after 72 hours, and serum from the father likewise showed the presence of toxoplasma-neutralizing antibodies, both as demonstrated on the rabbit skin and in vitro (1:16). Neither of the parents' sera contained toxoplasma complement-fixing antibodies.[13]

COMMENT

Except for the first well-authenticated case reported by Jankû from Prague, Czechoslovakia, in 1923,[5] the case reported herein is the earliest case of toxoplasmosis diagnosed from pathological material. Of course, without knowledge of the pioneer work of Wolf and Cowen[15] and of Sabin[10] and others, the diagnosis would not have been made at the present time.

The advanced lesions of toxoplasmosis observed in the patient at the age of five days are evidence of antenatal inception of the disease. Certain evidence has been collected[3] to support the thesis that most mothers when transmitting the disease are in the acute stage of toxoplasmic infection, rather than in a stage of latent chronicity, which is thought to follow the acute stage. The mother in this case was stated to have had pernicious vomiting of pregnancy while carrying the patient. However, although she had similar symptoms during a subsequent pregnancy, she gave birth to a normal child.

It was of interest to note the positive reaction to skin tests and the presence of neutralizing antibodies in the blood

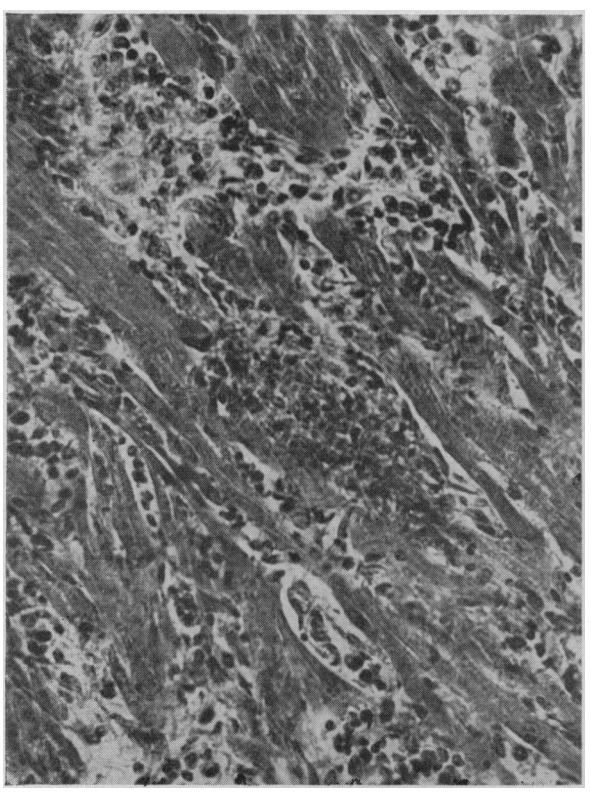

Figure 1.—Myocardial fibers showing necrosis, and infiltration by lymphocytes, plasma cells and larger mononuclear wandering cells; the endomysial fibroblasts are proliferating. Hematoxylin and eosin (x 325).

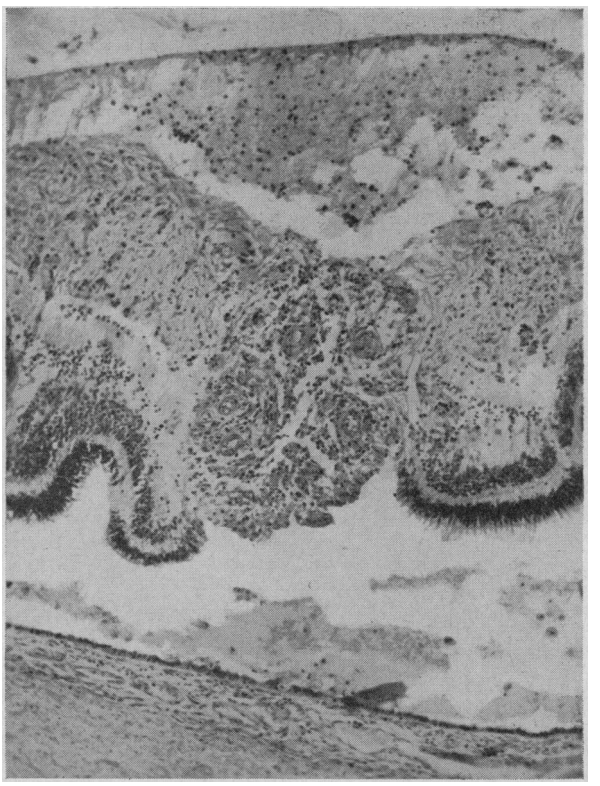

Figure 2.—Granulomatous retinitis (center) and slight choroiditis (below) with cellular exudate in vitreous (top) and between retina and choroid. Hematoxylin and eosin (x 80).

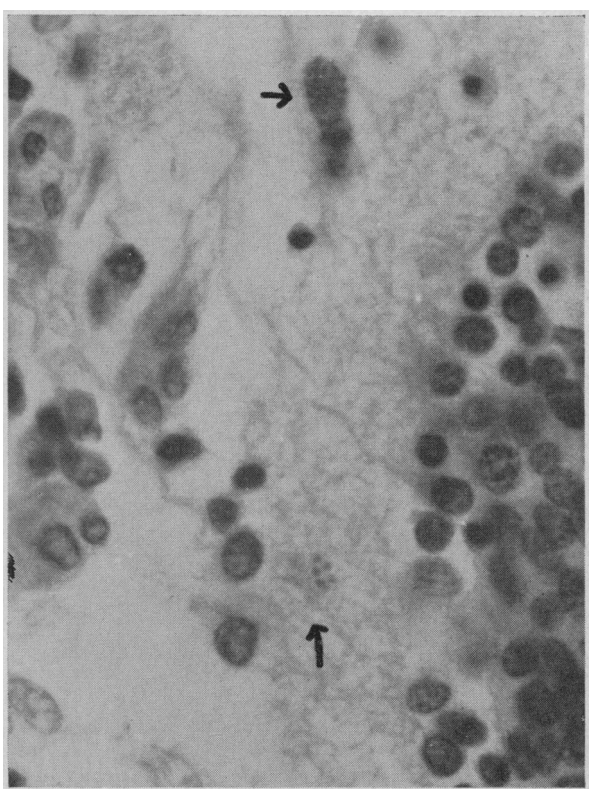

Figure 3.—Close-up of right center margin of area in Figure 2, showing two groups of toxoplasma in the outer fiber layer of the retina. Hematoxylin and eosin (x 845).

obtained from the parents. The date of the infection could not be determined. Such positive laboratory evidence of past toxoplasmic infection is frequently obtained in persons in an older age group.[2] A negative reaction to a toxoplasma complement-fixation test does not vitiate this observation, since such antibodies seem to disappear shortly after infection or the last contact with the antigen.[13, 3]

SUMMARY

A patient with congenital toxoplasmosis, fatal at five days of age, has been presented. The case is thought to be the earliest on record in the United States. The patient was observed at San Francisco, California, in 1923, and the diagnosis was made recently by finding toxoplasma and specific lesions in the pathologic material saved. Both parents, when examined in 1948, had positive reaction to the toxoplasmin skin test and the toxoplasma neutralizing antibody test.

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Pancreatic Cysts Simulating Carcinoma of the Head of the Pancreas

Report of Two Cases

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PANCREATICODUODENECTOMY as originally advocated in 1935 by Whipple[1] and his associates for the radical treatment of carcinoma of the papilla of Vater and the head of the pancreas has now become a recognized procedure. Although the early attempts to carry out this radical operation were associated with a high operative mortality, a better understanding of technique and of preoperative and postoperative care have made possible the radical resection of tumors involving the common bile duct, duodenum and head of the pancreas previously considered inoperable.

A number of modifications of the original two-stage operation as performed by Whipple have been made. With the use of vitamin K and blood transfusions to control hemorrhage and anemia, the trend is now toward a one-stage operation. Most surgeons now reimplant the cut end of the pancreas or pancreatic duct into the upper intestine to preserve the external pancreatic secretion, whereas Whipple considered this unnecessary and one of the main hazards of the procedure. Other modifications of the original procedure have to do mainly with the type and position of the anastomosis made to reestablish continuity and still prevent stenosis and troublesome regurgitation of bowel contents into the biliary tree.

With the technical problems solved, the main difficulty confronting the surgeon at present is one of early differential diagnosis. Unfortunately, a number of conditions involving both intra- and extrahepatic biliary passages give rise to similar clinical pictures and are extremely difficult to distinguish one from another. Too often the differential diagnosis is made late and surgical treatment undertaken when surgical extirpation is no longer feasible.

In general, the main consideration in diagnosis involves the differentiation between obstructive and non-obstructive jaundice, which unfortunately is occasionally impossible. In this connection, one must always keep in mind the frequent association of the two, particularly when obstructive jaundice itself has led to secondary degenerative changes in the liver.

Obstructive lesions of the extrahepatic biliary tree, both benign and malignant, although frequently easily distinguished one from the other, may produce clinical pictures so similar that positive differentiation cannot be made without exploratory laparotomy. For this reason it becomes imperative that the surgeon be prepared to recognize and undertake the surgical management of these lesions, regardless of their nature, as they present themselves in the operating room.

Unfortunately, gross and even microscopic examination at the time of operation will not always lead to a positive diagnosis. This is particularly true of obstructing lesions of the lower end of the common bile duct. Often a stone imbedded in the common duct near the ampulla of Vater, with inflammatory reaction about it, will simulate carcinoma. Carcinoma of the ampulla may cause stricture and obstruction without gross evidence of tumor. Inflammatory lesions of the pancreas often cause common duct obstruction and are grossly indistinguishable from carcinoma of the head of the pancreas, even with aid of frozen sections made at the time of operation.

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